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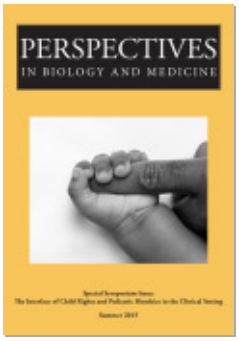

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Inducing HIV Remission in Neonates

child rights and research ethics

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ABSTRACT The U.N. Convention on the Rights of the Child (CRC) recognizes children as independent rights holders and articulates 38 substantive rights, including four general principles. It obligates states parties to realize these rights. The U.N. Committee on the Rights of the Child (Committee) oversees implementation of the CRC and can draw attention to areas requiring improvement. Many of the CRC's rights have implications for clinical research. While they justify some nontherapeutic research, they also require participants' protection. The Committee's guidance that decision-makers justify their decisions by reference to child rights has the potential to enrich the deliberations of research ethics committees. The CRC is consistent with requirements that low- and middle-income countries ensure that domestic research is relevant to the health needs of their populations and that resulting products and services are available to their populations. The CRC provides strong recognition of the role of parents and families and duties of states parties to support them in fulfilling their role. This could include support to improve informed consent processes.

International child rights law has the potential to change the way children are viewed and engaged by all social actors (Tobin 2012). It provides a child-cen-

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tered perspective on all areas of children's lives, including research with neonates. It differs from some bioethical perspectives by clearly articulating affirmative obligations owed to children and requiring rigorous monitoring mechanisms. The CRC's focus on affirmative obligations and establishment of monitoring mechanisms provide additional useful elements that are not present in the dominant form of American pediatric bioethics.

International Child Rights Law

An in-depth introduction to child rights and the U.N. Convention on the Rights of the Child (CRC) is presented by Lansdown, Lundy, and Goldhagen (2015) in their contribution to this volume. Adopted by the United Nations in 1989, the CRC encompasses civil and political, social, economic, cultural, recreational, and humanitarian rights, and it also contains a range of participation rights, including the right of children to have their views taken into account in decisions affecting them (Article 12) and to freedom of expression (Article 13). The 38 substantive rights apply to "every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier" (Article 1), regardless of age or capacities.

Four of the CRC rights serve as general principles: the right to non-discrimination (Article 2), the best interests principle (Article 3), the right to life, survival and development (Article 6), and respect for the views of the child (Article 12). Of relevance to this and other articles in this volume, in assessing the impact of any decision or measure, states are encouraged to use these four principles as an interpretative tool in the protection of the substantive rights of the CRC. The indivisibility of rights—in other words, the recognition that the fulfillment of one right may require the fulfillment of others—is also an important principle. For example, protection of children's right to health may also require the realization of their right to information (Article 13) and education (Articles 28 and 29).

In addition to the CRC, the Committee on the Rights of the Child (Committee) has issued General Comments on specific child rights issues, and three Optional Protocols that states can ratify independent of the CRC. These provide interpretive guidance and expand the depth and breadth of the principles of child rights. Of relevance to this case study, several General Comments provide detailed guidance on specific issues, such as HIV/AIDS, early childhood, and the highest attainable standard of health (UNCRC 2003, 2005, 2013b). With respect to Optional Protocols, No. 3 allows an individual child and the child's representatives to submit complaints to the Committee alleging violations of specific rights. After complaints are received, the Committee gives its views and recommendations to states parties, and the parties must report the actions taken to implement the Committee's recommendations (Article 11, UNCRC 2011). This provides a system of redress in international child rights law (DeBeco 2013).

A Child Rights Approach to Clinical Trials with Neonates

While the CRC makes no specific reference to clinical research, many of its rights are clearly relevant, such as the rights to life, survival, and development (Article 6), and to the highest attainable standard of health (Article 24). For example, in General Comment No. 15 on "The Right of the Child to the Enjoyment of the Highest Attainable Standard of Health" (para. 116), the Committee provides that states parties should seek to ensure good quality health services that are "scientifically and medically appropriate," as well as drugs and equipment that are child-specific. Article 24(2) sets out additional elements of the right to the highest attainable standard of health. Those which are most relevant to clinical research are the obligations on states to "diminish infant and child mortality" and to "combat disease and malnutrition." Furthermore, General Comment No. 15 (para. 34) states that particular attention must be paid to low birth weight, mother-to-child transmission of HIV, and neonatal infections.

Since the fulfillment of these obligations relies on clinical research, it can be argued that there is an obligation on states to encourage research. Furthermore, excluding children from clinical research and exposing them to the risks of extrapolating data from adults (Choonara 2004) can also be said to be a violation of states' obligations to protect children's rights to life, survival, and development and their right to the highest attainable standard of health.

Notwithstanding this argument, it should be noted that the permissibility of pediatric research that does not offer participants the prospect of direct benefit has been the subject of considerable bioethical debate. Since the CRC contends that "in all actions concerning children . . . the best interests of the child shall be a primary consideration" (Article 3), one might argue that nontherapeutic research is disallowed (Grover 2003). However, the Committee emphasizes that the best interests principle must be considered in both an "individual" and "collective" sense (UNCRC 2005). Additionally, the CRC states that the best interests of the child are to be regarded as "a" primary consideration: this indicates that the child's best interests are not to be considered as the single overriding factor and that the "collective, distributive justice-type dimension" of the principle must be acknowledged (Alston 1994). Clinical research is one area where the best interests standard should be interpreted in this manner, so as to permit some nontherapeutic research.

The rights of children in clinical trials must nonetheless also be protected. Legal and ethical instruments generally set a threshold of risk for nontherapeutic trials with children. For example, European Union law requires that such research will "pose only minimal risk to and will impose minimal burden on, the minor concerned in comparison to standard treatment for the minor's condition" (European Parliament and Council 2014, Article 32(g)(ii)); and U.S. law requires that research contain no more than a "minor increase over minimal risk" (HHS 2009,

section 46:406). Although there is considerable debate about the definition of these thresholds, it is sufficient to note that the risk to which children are exposed in research without the prospect of direct benefit must be subject to a defined "low" or "minimal" threshold, so that their rights to life, survival, development, and health are not compromised.

Trials relating to inducing HIV remission in neonates may have the prospect of direct benefit to participants. Neonates at risk of HIV may, however, need to be enrolled and treated prior to confirmation of their diagnosis. It is important—legally, ethically, and from a child rights perspective—to ensure that HIV-infected infants have access to the benefits of research and that uninfected infants are not harmed by the research.

In addition, from a child rights perspective, procedural clarity regarding the assessment of clinical trials is required. In relation to assessing and determining the best interests of a child or group of children, the Committee asserts, "States must develop transparent and objective processes for all decisions made by legislators, judges or administrative authorities, especially in areas which directly affect the child or children" (UNCRC 2013a, para. 87).

In assessing the best interests of the child or children, the unique position of the child or group of children must be considered and their rights must be weighed in the balance (UNCRC 2013a, 49–79). Decision-makers must also justify their decisions by articulating what is in the child's or children's best interests, the criteria for this determination, and how the child's or children's interests have been weighed against other considerations (UNCRC 2013a, 6a). The Committee states that these requirements should be followed in all "judicial and administrative decisions as well as in other actions concerning the child" (UNCRC 2013a, 10). Thus, it can be argued that research ethics committees or institutional review boards should undertake such rights-based decision-making procedures. This would enrich the process of risk/benefit assessment.

Ethical Requirements for Research in Lower-Income Countries

An additional issue in this case is whether the research should be conducted in high-income countries or low and middle-income countries. International bodies have developed a number of general principles for conducting research in lower-income countries. These requirements are not without controversy, and debates have arisen about their meaning (Wolitz, Emanuel, and Shah 2009). For example, research should be responsive to the health needs of host countries (CIOMS 2002; WMA 2013). This principle can be satisfied in the case under consideration, since the majority of infants affected with HIV live in low- and middle-income countries and the proposed trial may lead to the development of important treatments for these populations (Shah et al. 2014).

Participants in low- and middle-income countries may, however, be exploited if the interventions benefit only people in higher-income countries (Shah et al. 2014). Therefore, a second principle requires that any interventions should be made reasonably available to members of the community in which the research was conducted (CIOMS 2002). For example, Shah and colleagues argue that researchers should prospectively engage ministries of health, treatment programs, and international organizations to ensure that the research will meet the needs of the population.

While the CRC and its supporting instruments do not provide direct guidance on research in low- and middle-income countries, General Comment No. 3 on HIV/AIDs recognizes that "States parties must ensure that HIV/AIDS research programs include specific studies that contribute to effective prevention, care, treatment and impact reduction for children" (UNCRC 2003, para. 29). It argues that there is an obligation on states parties to take steps to provide essential treatment, such as "anti-retroviral drugs, appropriate antenatal, delivery and post-partum care" (para. 26), and mentions that they should negotiate with the pharmaceutical industry to make necessary medicines available (para. 28). Thus, it can be argued that there is an obligation on low- and middle-income countries to seek to ensure that the research is relevant to the health needs of their populations and that any medicines or treatments that result from such research will be made available to their populations.

It is important to ensure that the rights of neonates are afforded the same protection in lower-income countries as in higher-income countries. Neonates should not be exposed to risks without having access to the possible benefits of the research. Such a practice would be a breach of the rights of neonates to be protected from all forms of discrimination (Article 2) and from exploitation (Article 36).

Informed Consent

Legal and ethical mandates require consent from a person with parental authority for the involvement of children in research (WMA 2013). One of the issues in this case relates to potential barriers to obtaining adequately informed consent. If the research is conducted in low- or middle-income countries, the parents may have lower health literacy. Additionally, obtaining consent during labor is less than ideal, given the stresses of the situation.

From a child rights perspective, parents and families are given strong recognition in the realization of child rights (Article 5). The CRC fully supports parents in nurturing, protecting, and guiding their children, and it also sets out corresponding state obligations (Cantwell 2007). Specifically, Article 18(1) states that parents' "basic concern" will be the best interests of their child, and the second element of Article 18(2) states that "States Parties shall render appropriate assistance

to parents and legal guardians in the performance of their child-rearing responsibilities and shall ensure the development of institutions, facilities and services for the care of children." Thus, measures to support parents or guardians in realizing the rights of neonates are required.

In this case, obtaining consent during prenatal care would be preferable, because it would allow pregnant women more time for consideration. If it were only possible to obtain informed consent during labor, additional assistance would be particularly relevant. The use of independent advocates could help to ensure that there is no confusion or misunderstanding about the trial, and their involvement may also reduce the chance that feelings of obligation towards health professionals or power imbalances would inappropriately influence decisions. The use of independent advocates can help to fulfill parental obligations towards their children under Article 18 of the CRC, and indirectly can also be viewed as a way in which to realize the right to participation of the neonate under Article 12.

Conclusion

The CRC represents a milestone for child rights and can enrich bioethics through the principle that children are independent bearers of rights and that there are obligations on states and state bodies regarding the fulfillment of those rights. The CRC strikes a balance between group and individual rights and requires procedural clarity: it emphasizes equal respect for children as rights-bearers and ensures that they receive consistent protection and benefits, regardless of the setting. The CRC also recognizes the need for additional support for certain children in the protection of their rights. In the case of HIV remission research in neonates, it emphasizes the rights of all children, including those in lower-income countries, to access to the benefits of research, protection in the conduct of research, procedural clarity in the review of study protocols, and support of parents in providing informed consent.

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